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L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:626076 HCAPLUS  
 DOCUMENT NUMBER: 131:248270  
 TITLE: Remedies for **hepatitis**  
 INVENTOR(S): **Hirabayashi, Kazuko; Seki, Junzo**  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948531	A1	19990930	WO 1999-JP1438	19990323
W: AU, BR, CA, CN, HU, ID, IL, JP, KR, MX, NO, NZ, RU, UA, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2325550	AA	19990930	CA 1999-2325550	19990323
AU 9928550	A1	19991018	AU 1999-28550	19990323
EP 1064950	A1	20010103	EP 1999-909297	19990323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

## PRIORITY APPLN. INFO.:

JP 1998-76055 A 19980324  
 WO 1999-JP1438 W 19990323

AB The invention relates to novel drugs [liposomes] efficacious in treating and preventing **hepatitis**. These drugs are remedies or preventives for **hepatitis** characterized by contg. a complex of a drug carrier comprising as the essential components, for example, 2-0-(2-diethylaminoethyl)carbamoyl-1,3,0-dioleoyl glycerol and a phospholipid with poly(I).poly(C).

IT **24936-38-7**, Poly(A).poly(U) **24939-03-5**, Poly(I).poly(C)  
**160005-13-0**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (remedies for treatment of **hepatitis**)

RN **24936-38-7** HCAPLUS

CN 5'-Adenylic acid, homopolymer, complex with 5'-uridylic acid homopolymer  
 (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 27416-86-0

CMF (C9 H13 N2 O9 P)x

CCI PMS

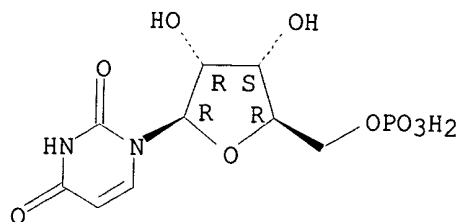
CM 2

CRN 58-97-9

CMF C9 H13 N2 O9 P

CDES 5:B-D-RIBO

Absolute stereochemistry.



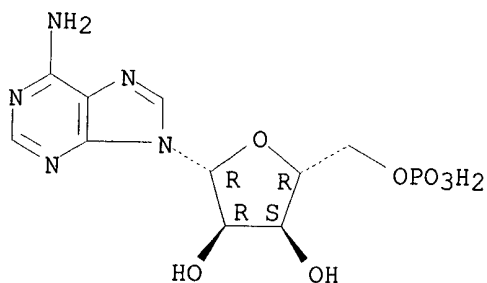
CM 3

CRN 24937-83-5  
 CMF (C10 H14 N5 O7 P)x  
 CCI PMS

CM 4

CRN 61-19-8  
 CMF C10 H14 N5 O7 P  
 CDES 5:B-D-RIBO

Absolute stereochemistry.



RN 24939-03-5 HCAPLUS  
 CN 5'-Inosinic acid, homopolymer, complex with 5'-cytidylic acid homopolymer  
 (1:1) (9CI) (CA INDEX NAME)

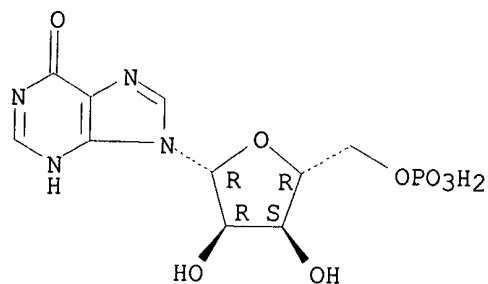
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CRN 30918-54-8  
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 CCI PMS

CM 2

CRN 131-99-7  
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 CDES 5:B-D-RIBO

Absolute stereochemistry.



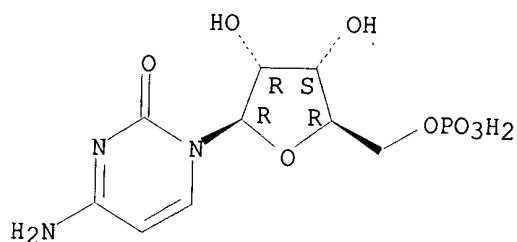
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CRN 30811-80-4  
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 CCI PMS

CM 4

CRN 63-37-6  
 CMF C9 H14 N3 O8 P  
 CDES 5:B-D-RIBO

Absolute stereochemistry.

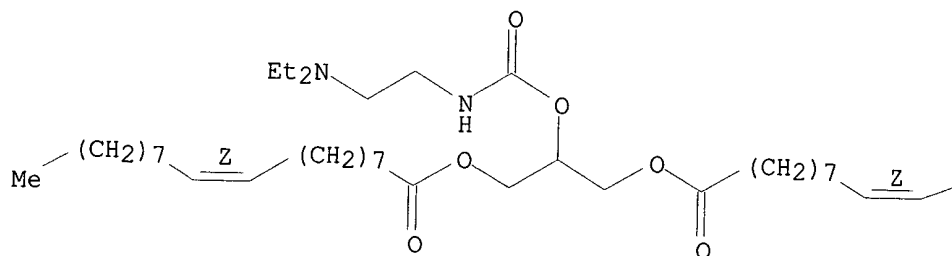


RN 160005-13-0 HCAPLUS

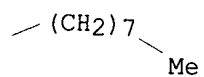
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-  
 1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'REGISTRY' ENTERED AT 11:56:04 ON 24 JUN 2002)

DEL HIS

L1 0 S 160005-13-0/CRN  
L2 1 S 160005-13-0/RN  
L3 4 S 24939-03-5/CRN  
L4 3 S 24936-38-7/CRN  
L5 0 S L2 AND L3 AND L4  
L6 1 S 24939-03-5/RN  
L7 1 S 24936-38-7/RN  
L8 0 S L2 AND L6 AND L7

*- Reg. No. for compd. requested*

FILE 'HCAPLUS' ENTERED AT 12:50:08 ON 24 JUN 2002

L9

8 S L2

*8 cits for compd. requested - attached*

FILE 'CAOLD' ENTERED AT 12:51:18 ON 24 JUN 2002

L10

0 S L2

*Onits in CAOLD*

FILE 'HCAPLUS' ENTERED AT 12:54:15 ON 24 JUN 2002

L11

2 S L9 AND HEPATITIS

*mention  
2 cits specifically ~~th~~ hepatitis -  
see yellow tab*

=&gt; d 19 ibib abs hitstr 1-8

L9 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:765838 HCAPLUS

DOCUMENT NUMBER: 134:357478

TITLE: Inhibition of metastatic carcinoma cell growth in  
livers by poly(I):poly(C)/cationic liposome complex  
(LIC)AUTHOR(S): Hirabayashi, Kazuko; Yano, Junichi; Takesue, Hisashi;  
Fujiwara, Noriko; Irimura, TatsuroCORPORATE SOURCE: Discovery Research Laboratories, Nippon Shinyaku Co.  
Ltd., Kyoto, 601-8550, JapanSOURCE: Oncology Research (1999), 11(11/12), 497-504  
CODEN: ONREE8; ISSN: 0965-0407

PUBLISHER: Cognizant Communication Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The complex of poly(I):poly(C) and a new cationic liposome (LIC) has a potent antitumor activity against many tumor cell lines in vitro, whereas poly(I):poly(C) itself has no such activity. In the present study we tested the sensitivity of 21 human colon and pancreatic cancer cell lines to LIC or Adriamycin in vitro. The growth of most of the cell lines was strongly inhibited by both LIC and Adriamycin in vitro, although a few insensitive cell lines were different. We also studied the in vivo antitumor activity of LIC or Adriamycin in three exptl. liver metastasis models in nude mice using a human pancreatic cancer cell line (AsPC-1) and two human colon cancer cell lines (Ls174T and HCC-M1544). The administration of LIC or Adriamycin was started 3 days after the injection of tumor cells. Animals received 0.1 mg/kg LIC IV twice weekly or 5 mg/kg Adriamycin IV every 5 days during the expts. LIC showed potent antitumor activity in all three liver cancer models. Although Adriamycin had potent antitumor activity in the HCC-M1544 model, it had only a moderate effect in the AsPC-1 model and at most a weak effect in the Ls174T model. At the EDs LIC did not cause detectable pathol. changes in the liver and did not elicit toxicity to mice in these models, whereas Adriamycin did exhibit toxic effects. These results suggest that LIC is a promising candidate drug to treat hepatic metastasis.

IT 160005-13-0

RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

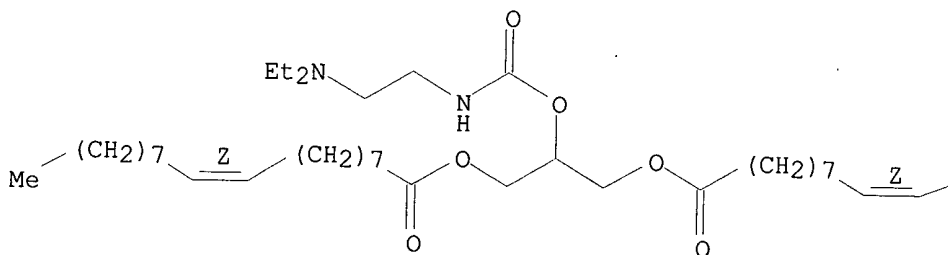
(inhibition of metastatic carcinoma cell growth in livers by  
poly(I):poly(C)/cationic liposome complex)

RN 160005-13-0 HCAPLUS

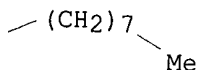
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-  
1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:573814 HCAPLUS  
 DOCUMENT NUMBER: 133:164271  
 TITLE: Shortened-chain polynucleotides and process for the preparation thereof  
 INVENTOR(S): Matsuyama, Shinji; Ishiyama, Kouichi; Seki, Junzo; Ohgi, Tadaaki  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co. Ltd., Japan  
 SOURCE: PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047601	A1	20000817	WO 2000-JP778	20000214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000008227	A	20011030	BR 2000-8227	20000214
EP 1153931	A1	20011114	EP 2000-902934	20000214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001003941	A	20010814	NO 2001-3941	20010814
PRIORITY APPLN. INFO.:				
			JP 1999-35963	A 19990215
			WO 2000-JP778	W 20000214

AB Specifically, shortened-chain polynucleotides or salts thereof, characterized by the content of 2'-5' phosphoric diester linkage of 3 % or below based on all the phosphoric diester linkages and medicinal compns. contg. both are prepd. by thermal hydrolysis of polynucleotides or salts thereof or enzymic hydrolysis with phosphodiesterase. These shortened-chain polynucleotides are useful as drugs such as interferon inducers, immunostimulants, cellular nuclease activators, or anticancer agents or preventives or therapeutic agents for hepatitis. Anticancer activity of shortened-chain polyinosinic acid-polycytidylic acid duplexes against HeLa S3 cells strongly correlated to the chain length and the chain length of .gtoreq.1,000 bases exhibited the most potent

anti-proliferation activity but shortened-chain duplexes with av. chain length of 100-1,000 bases also exhibited slightly lower but strong enough anticancer activity. The larger ratio of trans-phosphorylation from 3' to 2'-position weakened anticancer activity of polyinosinic acid and polycytidylic acid against A431 cells. Thus, 8 g inosine-5'-diphosphate trisodium salt and 1 g  $MgCl_2$  were dissolved in 500 mL 0.1 M glycine-NaOH buffer soln. with stirring, followed by adjusting the pH of the soln. at 9.3 with 6 N NaOH, allowing the soln. to stand at 38.degree. for 1 h, and adding polynucleotide phosphorylase, and the resulting mixt. was allowed to react at 38.degree. for 18 h. The reaction was quenched by adding 25 mL 0.2 M EDTA, followed by adding 10 mL satd. NaCl soln. and 500 mL anhyd. EtOH to ppt. polyinosinic acid which was sepd. by centrifugation. The polyinosinic acid ppt. was redissolved in water and dialyzed, treated with activated charcoal, and filtered. The filtrate was adjusted to pH 8.5 with 6 N NaOH and heated at 70.degree. for 8 h to give polyinosinic acid Na salt (av. chain length of 360 bases). The above polyinosinic acid salt and polycytidylic acid sodium salt (av. chain length 318 bases) (prepn. given) were added to cationic liposome, which was prepd. from 2-O-(2-diethylaminoethyl)carbamoyl-1,3-O-dioleoylglycerol and egg yoke lecithin, under stirring and dispersed to give a polynucleotide complex, which in vitro inhibited the proliferation of HeLa S3 cells by 17, 70, and 100% at 0.1, 1, and 10 (polyinosinic acid salt + polycytidylic acid sodium salt) ng/mL, resp.

IT 160005-13-0P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

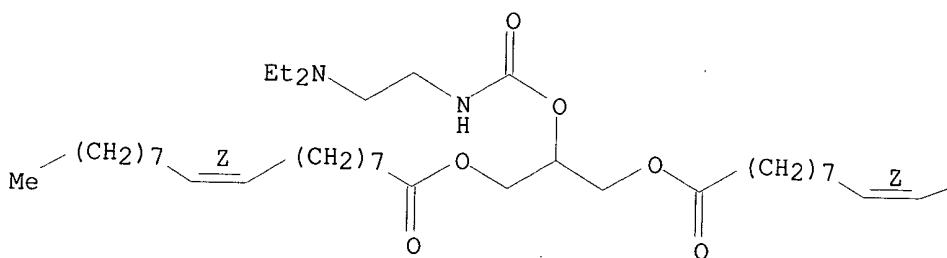
(cationic liposome contg. poly[I].poly[C] complex and; prepn. of shortened-chain polynucleotides interferon inducers, immunostimulants, cellular nuclease activators, or anticancer agents or preventives or therapeutic agents for hepatitis)

RN 160005-13-0 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

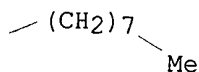
Double bond geometry as shown.

PAGE 1-A





PAGE 1-B



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:763878 HCAPLUS  
 DOCUMENT NUMBER: 132:6370  
 TITLE: Process for producing composite preparation containing nucleic acid  
 INVENTOR(S): Sugihara, Katsuhiko; Seki, Junzo; Hirabayashi, Kazuko  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961032	A1	19991202	WO 1999-JP2713	19990524
W: CA, CN, JP, KR, RU, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1086699	A1	20010328	EP 1999-921242	19990524
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

JP 1998-142763 A 19980525  
 WO 1999-JP2713 W 19990524

AB A process for producing a homogeneous nucleic-acid-contg. composite prepn. of good quality which is capable of sterilization by filtration and is characterized by contg. no coarse particles having a size of .gtoreq. 7 .mu.m, which are regarded as unsafe for the human body. The process for producing the prepn., contg. a composite of a cationic carrier with a nucleic acid polymer, is characterized in that two single-stranded nucleic acid polymers capable of at least partly forming a double-stranded state are sep. added, each in the single-stranded state, to either a cationic carrier or a material from which the cationic carrier is to be formed, and all these ingredients are subjected to a dispersing treatment. A freeze-dried compn. was prepd. from 2-O-(2-diethylaminoethyl)-carbamoyle-1,3-O-diethylglycerol, egg lecithin, water, poly(I) (polyinosinic acid), and poly(C) (polycytidylic acid). The av. particle size of the composite particles after dissolved in injection water was 140 nm.

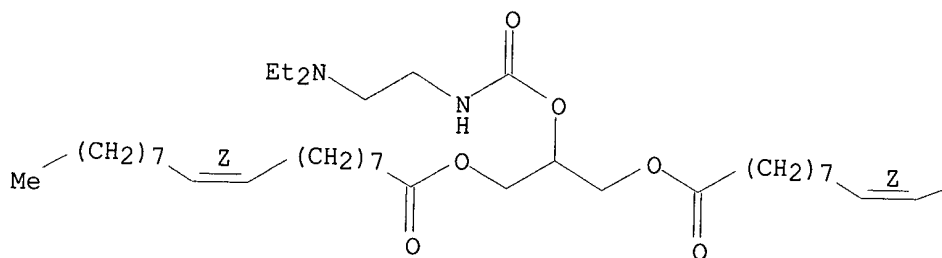
IT 160005-13-0, 2-O-(2-Diethylaminoethyl)-carbamoyle-1,3-O-diethylglycerol  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compn. contg. two single-stranded nucleic acid polymers and cationic carrier)

RN 160005-13-0 HCAPLUS

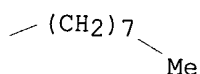
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:626076 HCAPLUS  
 DOCUMENT NUMBER: 131:248270  
 TITLE: Remedies for hepatitis  
 INVENTOR(S): Hirabayashi, Kazuko; Seki, Junzo  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948531	A1	19990930	WO 1999-JP1438	19990323
W: AU, BR, CA, CN, HU, ID, IL, JP, KR, MX, NO, NZ, RU, UA, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2325550	AA	19990930	CA 1999-2325550	19990323
AU 9928550	A1	19991018	AU 1999-28550	19990323
EP 1064950	A1	20010103	EP 1999-909297	19990323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

JP 1998-76055 A 19980324  
 WO 1999-JP1438 W 19990323

AB The invention relates to novel drugs [liposomes] efficacious in treating

and preventing hepatitis. These drugs are remedies or preventives for hepatitis characterized by contg. a complex of a drug carrier comprising as the essential components, for example, 2-0-(2-diethylaminoethyl)carbamoyl-1,3,0-dioleoyl glycerol and a phospholipid with poly(I).poly(C).

IT 160005-13-0

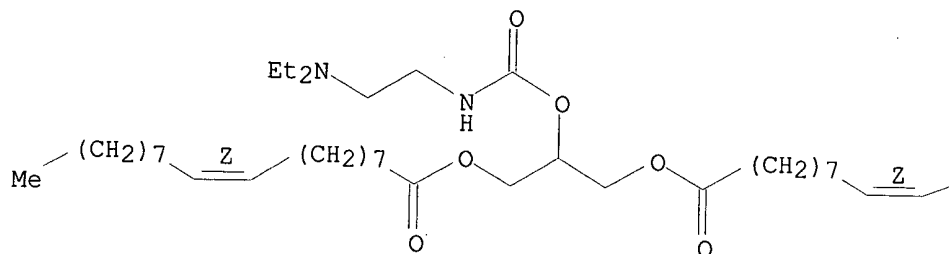
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(remedies for treatment of hepatitis)

RN 160005-13-0 HCAPLUS

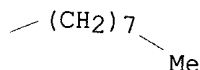
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:580519 HCAPLUS  
 DOCUMENT NUMBER: 131:314154  
 TITLE: Inhibition of cancer cell growth by polyinosinic-polycytidylic acid/cationic liposome complex: a new biological activity  
 AUTHOR(S): Hirabayashi, Kazuko; Yano, Junichi; Inoue, Toshihiko; Yamaguchi, Tohru; Tanigawara, Kazuaki; Smyth, Gerald E.; Ishiyama, Kouichi; Ohgi, Tadaaki; Kimura, Kiyoshi; Irimura, Tatsuro  
 CORPORATE SOURCE: Discovery Research Laboratories, Nippon Shinyaku Co., Ltd., Kyoto, 601-8550, Japan  
 SOURCE: Cancer Research (1999), 59(17), 4325-4333  
 CODEN: CNREA8; ISSN: 0008-5472  
 PUBLISHER: AACR Subscription Office  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A complex of polyinosinic-polycytidylic acid [poly(I).cntdot.poly(C)] and

cationic liposome (LIC) inhibited the growth of many tumor cell lines at low concn. in vitro, but poly(I).cntdot.poly(C) alone had no such antiproliferative effect. The IC50 values of LIC against the tumor cells ranged from 0.1 to 1000 ng/mL. LIC had strong cytotoxic effects on malignant cells of epithelial and fibroblastic origin from various tissues and was also effective against Adriamycin-resistant tumor cells. LIC did not significantly affect the growth of lymphoma cells, leukemia cells, normal diploid fibroblasts, or primary liver cells at concns. up to 10 .mu.g/mL. The mechanism of the antiproliferative effect of LIC against malignant cells was the induction of apoptosis. LIC induced the fragmentation of nuclear DNA and the degrdn. of rRNA in tumor cells. The DNA fragmentation occurred within 1-5 h after the addn. of LIC, and both the fragmentation and the inhibition of cancer-cell growth were suppressed by a nuclease inhibitor. In contrast, caspase inhibitors did not affect the antiproliferative activity of LIC. These results suggest that LIC induced apoptosis in malignant cells through the direct activation of nucleases and not through the activation of caspases. LIC reduced the incidence and the size of metastatic liver-cancer tumors in two different mouse metastatic liver-cancer models using human colon carcinoma cells. Histochem. anal. revealed that the KM12-HX cells in the tumor nodules were undergoing apoptosis; therefore, LIC also induced the apoptosis of tumor cells in vivo. In these animal models, LIC caused no obsd. changes in normal hepatocytes.

IT 160005-13-0

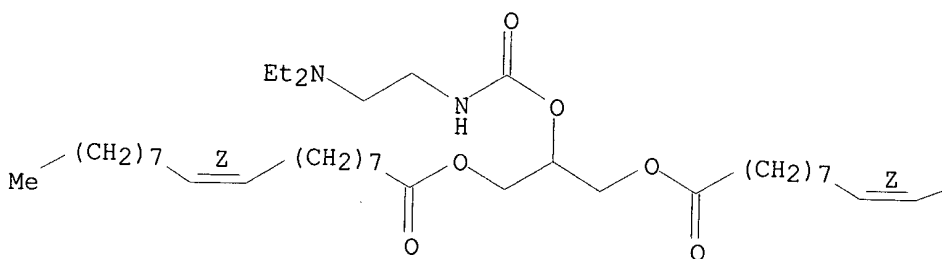
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (liposomes contg.; inhibition of cancer cell growth by polyinosinic-polycytidylic acid/cationic liposome complex)

RN 160005-13-0 HCAPLUS

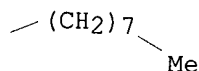
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

Searched by Mary Jane Ruhl 605-1155

Page 7

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:282104 HCAPLUS  
 DOCUMENT NUMBER: 130:287086  
 TITLE: Intra-cancer-cell nuclease activator  
 INVENTOR(S): Hirabayashi, Kazuko; Seki, Junzo  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920283	A1	19990429	WO 1998-JP4695	19981015
W: AU, BR, CA, CN, HU, ID, IL, JP, KR, MX, NO, NZ, RU, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9809432	A	19990416	ZA 1998-9432	19981015
CA 2306085	AA	19990429	CA 1998-2306085	19981015
AU 9894626	A1	19990510	AU 1998-94626	19981015
AU 743137	B2	20020117		
EP 1029544	A1	20000823	EP 1998-947915	19981015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

## PRIORITY APPLN. INFO.:

JP 1997-283968 A 19971016  
 WO 1998-JP4695 W 19981015

AB The invention relates to a drug efficacious for cancer therapy and a novel drug contg. a double-stranded RNA such as poly(I).poly(C). Specifically, an intra-cancer-cell nuclease activator contg. 2-O-(2-diethylaminoethyl)-carbamoyl-1,3-O-diethylglycerol and a composite comprising a carrier prepd. from a phospholipid as an essential component and poly(I).poly(C) or mismatched poly(I).poly(C).

IT 160005-13-0, 2-O-(2-Diethylaminoethyl)-carbamoyl-1,3-O-diethylglycerol

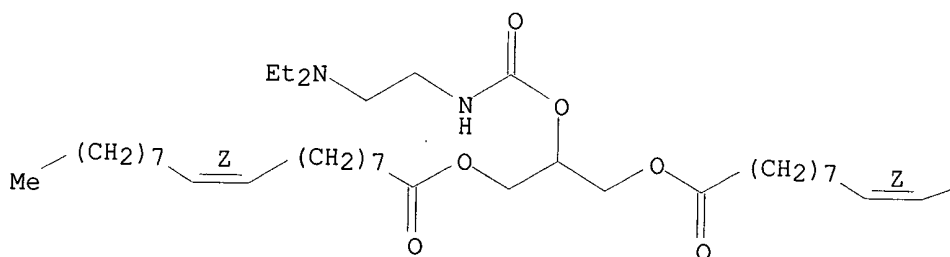
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (intra-cancer-cell nuclease activator)

RN 160005-13-0 HCAPLUS

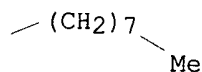
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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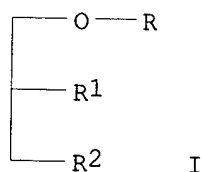
PAGE 1-B



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:528415 HCAPLUS  
 DOCUMENT NUMBER: 122:291443  
 TITLE: preparation of glycerol derivatives for a drug delivery device  
 INVENTOR(S): Yano, Junichi; Ohgi, Tadaaki  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 94 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9419314	A1	19940901	WO 1994-JP237	19940217
W: AU, BR, CA, CN, FI, HU, JP, KR, NO, NZ, RU, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2156288	AA	19940901	CA 1994-2156288	19940217
CA 2156289	AA	19940901	CA 1994-2156289	19940217
AU 9460449	A1	19940914	AU 1994-60449	19940217
EP 685457	A1	19951206	EP 1994-907060	19940217
EP 685457	B1	19991215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE				
RU 2123492	C1	19981220	RU 1995-121693	19940217
JP 2924179	B2	19990726	JP 1994-518814	19940217
AT 187713	E	20000115	AT 1994-907060	19940217
ES 2142934	T3	20000501	ES 1994-907060	19940217
JP 3189279	B2	20010716	JP 1994-518815	19940217
US 6020317	A	20000201	US 1995-507518	19951023
PRIORITY APPLN. INFO.:			JP 1993-54939	A 19930219
			WO 1994-JP237	W 19940217
OTHER SOURCE(S):		CASREACT 122:291443; MARPAT 122:291443		
GI				



AB Glycerol derivs. I [R1, R2 = OY, A-(CH<sub>2</sub>)<sub>n</sub>-E; n = 0-4; E = pyrrolidino, piperidino, (un)substituted piperazino, morpholino, (un)substituted guanidino, (un)substituted amino; A = -O-CO-NH-, -NH-CO-O-, -O-CO-, etc.; R, Y = C10-30 (un)satd. aliph. hydrocarbyl, C10-30 (un)satd. aliph. acid residue] are prepd. Thus, 1,2-O-dioleoylglycerol in pyridine was stirred with N,N'-carbonyldiimidazole at room temp. for 5 h, the resulting was dissolved in CH<sub>2</sub>Cl<sub>2</sub>, washed with 5% NaH<sub>2</sub>PO<sub>3</sub>, the product was dissolved in DMF, N,N-dimethylethylenediamine was added, and the resulting mixt. was stirred overnight to give 91% the title compd. 3-O-(2-dimethylaminoethyl)carbamoyl-1,2-O-dioleoylglycerol. The invention aims at providing a device comprising lipids that act like the so-called cationic liposome and are reduced in toxicity and the lipids as the constituent of the device. The invention compds. are exemplified by 3-O-(4-dimethylaminobutanoyl)-1,2-O-dioleoylglycerol, 3-O-(2-dimethylaminoethyl)carbamoyl-1,2-O-dioleoylglycerol, 3-O-(2-diethylaminoethyl)carbamoyl-1,2-O-dioleoylglycerol, and 2-O-(2-diethylaminoethyl)-carbamoyl-1,3-O-dioleoylglycerol. The device comprises these lipids and phospholipids. The device enables, when administered to with, for example, a double-stranded RNA, the RNA to migrate to the action site safely.

IT 160005-13-0P

RL: DEV (Device component use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)

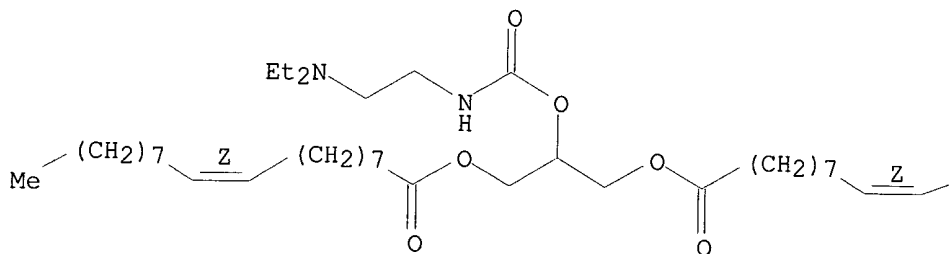
(prepn. of glycerol derivs. for a drug delivery device)

RN 160005-13-0 HCAPLUS

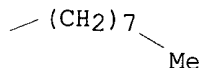
CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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L9 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:274951 HCAPLUS  
 DOCUMENT NUMBER: 122:64335  
 TITLE: antitumor compositions containing nucleic acid

INVENTOR(S): copolymer and lipid device  
 Yano, Junichi; Ohgi, Tadaaki  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 85 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418987	A1	19940901	WO 1994-JP238	19940217
W: AU, BR, CA, CN, FI, HU, JP, KR, NO, NZ, RU, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2156288	AA	19940901	CA 1994-2156288	19940217
CA 2156289	AA	19940901	CA 1994-2156289	19940217
AU 9460450	A1	19940914	AU 1994-60450	19940217
EP 685234	A1	19951206	EP 1994-907061	19940217
EP 685234	B1	20000510		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE				
RU 2143903	C1	20000110	RU 1995-121696	19940217
ES 2142934	T3	20000501	ES 1994-907060	19940217
AT 192657	E	20000515	AT 1994-907061	19940217
JP 3189279	B2	20010716	JP 1994-518815	19940217
US 5705188	A	19980106	US 1995-507269	19951010
PRIORITY APPLN. INFO.:				
			JP 1993-54939	A 19930219
			WO 1994-JP238	W 19940217

OTHER SOURCE(S): MARPAT 122:64335

AB Pharmaceutical comps. comprise a single-stranded nucleic acid copolymer, esp. poly(adenylic acid-uridylic acid), and a lipid device [such as lipofecting (com. product) on a mixt. contg. phospholipid and glycerol derivs. such as 3-O-(4-dimethylaminobutanoyl)-1,2-O-dioleoylglycerol]. The lipid device promoted the entrance of single-stranded nucleic acid into tumor cells to induce interferon activity. As a result, the nucleic acid copolymer acted as neoplasm inhibitor. An injection was formulated contg. poly(adenylic acid-uridylic acid) and the lipid device is saline.

IT 160005-13-0P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

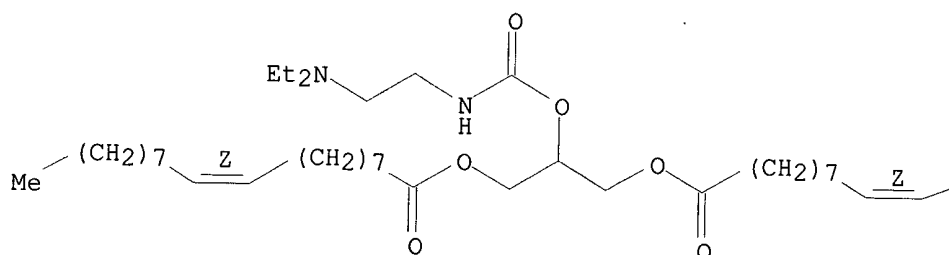
(antitumor comps. contg. nucleic acid copolymer and lipid device)

RN 160005-13-0 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, 2-[[[2-(diethylamino)ethyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





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